

What is claimed is:

1. An isolated nucleic acid molecule selected from the group consisting of:

5 a) a nucleic acid molecule comprising a nucleotide sequence which is at least 60% homologous to the nucleotide sequence of SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:12, the DNA insert of the plasmid deposited with ATCC as Accession Number \_\_\_\_\_ or \_\_\_\_\_, or a complement thereof;

10 b) a nucleic acid molecule comprising a fragment of at least 537 nucleotides of a nucleic acid comprising the nucleotide sequence of SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:12, the DNA insert of the plasmid deposited with ATCC as Accession Number \_\_\_\_\_ or \_\_\_\_\_, or a complement thereof;

15 c) a nucleic acid molecule which encodes a polypeptide comprising an amino acid sequence at least about 60% homologous to the amino acid sequence of SEQ ID NO:5, SEQ ID NO:8, or SEQ ID NO:11, or an amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number \_\_\_\_\_ or \_\_\_\_\_;

20 d) a nucleic acid molecule which encodes a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:5, SEQ ID NO:8, or SEQ ID NO:11, or the polypeptide encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number \_\_\_\_\_ or \_\_\_\_\_, wherein the fragment comprises at least 15 contiguous amino acid residues of the amino acid sequence of SEQ ID  
25 NO:5, SEQ ID NO:8, or SEQ ID NO:11, or the polypeptide encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number \_\_\_\_\_ or \_\_\_\_\_; and

30 e) a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:5, SEQ ID NO:8, or SEQ ID NO:11, or an amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number \_\_\_\_\_ or \_\_\_\_\_, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule comprising SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:10, or SEQ ID NO:12 under stringent conditions.

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2. The isolated nucleic acid molecule of claim 1 which is selected from the group consisting of:

a) a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:10, or SEQ ID NO:12 or the DNA insert of the plasmid deposited with ATCC as Accession Number \_\_\_\_\_ or \_\_\_\_\_, or a complement thereof; and

5 b) a nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:5, SEQ ID NO:8, or SEQ ID NO:11, or an amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number \_\_\_\_\_ or \_\_\_\_\_.

10 3. The nucleic acid molecule of claim 1 further comprising vector nucleic acid sequences.

4. The nucleic acid molecule of claim 1 further comprising nucleic acid sequences encoding a heterologous polypeptide.

15 5. A host cell which contains the nucleic acid molecule of claim 1.

6. The host cell of claim 5 which is a mammalian host cell.

20 7. A non-human mammalian host cell containing the nucleic acid molecule of claim 1.

8. An isolated polypeptide selected from the group consisting of:

25 a) a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:5, SEQ ID NO:8, or SEQ ID NO:11, or the polypeptide encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number \_\_\_\_\_ or \_\_\_\_\_, wherein the fragment comprises at least 15 contiguous amino acids of SEQ ID NO:5, SEQ ID NO:8, or SEQ ID NO:11, or the amino acid sequence encoded by  
30 the DNA insert of the plasmid deposited with ATCC as Accession Number \_\_\_\_\_ or \_\_\_\_\_;

b) a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:5, SEQ ID NO:8, or SEQ ID NO:11, or an amino acid sequence encoded by the DNA insert of the plasmid deposited with  
35 ATCC as Accession Number \_\_\_\_\_ or \_\_\_\_\_, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to a nucleic acid molecule comprising SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:10, or SEQ ID NO:12 under stringent conditions; and

5 c) a polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence which is at least 60% homologous to a nucleic acid comprising the nucleotide sequence of SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:10, or SEQ ID NO:12, or the DNA insert of the plasmid deposited with ATCC as Accession Number \_\_\_\_\_ or \_\_\_\_\_.

10 d) a polypeptide comprising an amino acid sequence which is at least 60% homologous to the amino acid sequence of SEQ ID NO:5, SEQ ID NO:8, or SEQ ID NO:11, or the polypeptide encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number \_\_\_\_\_ or \_\_\_\_\_.

9. The isolated polypeptide of claim 8 comprising the amino acid sequence of SEQ ID NO:5, SEQ ID NO:8, or SEQ ID NO:11, or an amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number \_\_\_\_\_ or \_\_\_\_\_.

15 10. The polypeptide of claim 8 further comprising heterologous amino acid sequences.

11. An antibody which selectively binds to a polypeptide of claim 8.

20 12. A method for producing a polypeptide selected from the group consisting of:  
a) a polypeptide comprising the amino acid sequence of SEQ ID NO:5, SEQ ID NO:8, or SEQ ID NO:11, or an amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number \_\_\_\_\_ or \_\_\_\_\_;

25 b) a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:5, SEQ ID NO:8, or SEQ ID NO:11, or an amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number \_\_\_\_\_ or \_\_\_\_\_ wherein the fragment comprises at least 15 contiguous amino acids of SEQ ID NO:5, SEQ ID NO:8, or SEQ ID NO:11, or the amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as  
30 Accession Number \_\_\_\_\_ or \_\_\_\_\_; and

35 c) a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:5, SEQ ID NO:8, or SEQ ID NO:11, or an amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number \_\_\_\_\_ or \_\_\_\_\_, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to a nucleic acid molecule comprising SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:10, or SEQ ID NO:12 under stringent conditions;

comprising culturing the host cell of claim 5 under conditions in which the nucleic acid molecule is expressed.

- 5           13.    A method for detecting the presence of a polypeptide of claim 8 in a sample comprising:
- a)    contacting the sample with a compound which selectively binds to the polypeptide; and
  - b)    determining whether the compound binds to the polypeptide in the sample to thereby detect the presence of a polypeptide of claim 8 in the sample.

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          14.    The method of claim 13, wherein the compound which binds to the polypeptide is an antibody.

- 15           15.    A kit comprising a compound which selectively binds to a polypeptide of claim 8 and instructions for use.

16.    A method for detecting the presence of a nucleic acid molecule in claim 1 in a sample comprising:
- a)    contacting the sample with a nucleic acid probe or primer which selectively hybridizes to the nucleic acid molecule; and
  - b)    determining whether the nucleic acid probe or primer binds to a nucleic acid molecule in the sample to thereby detect the presence of a nucleic acid molecule of claim 1 in the sample.

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- 25           17.    The method of claim 16, wherein the sample comprises mRNA molecules and is contacted with a nucleic acid probe.

18.    A kit comprising a compound which selectively hybridizes to a nucleic acid molecule of claim 1 and instructions for use.

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19.    A method for identifying a compound which binds to a polypeptide of claim 8 comprising:
- a)    contacting the polypeptide, or a cell expressing the polypeptide with a test compound; and
  - b)    determining whether the polypeptide binds to the test compound.

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          20.    The method of claim 19, wherein the binding of the test compound to the polypeptide is detected by a method selected from the group consisting of:

- a) detection of binding by direct detection of test compound/polypeptide binding;
- b) detection of binding using a competition binding assay; and
- c) detection of binding using an assay for TWIK activity.

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21. A method for modulating the activity of a polypeptide of claim 8 comprising contacting the polypeptide or a cell expressing the polypeptide with a compound which binds to the polypeptide in a sufficient concentration to modulate the activity of the polypeptide.

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22. A method for identifying a compound which modulates the activity of a polypeptide of claim 8 comprising:

- a) contacting a polypeptide of claim 8 with a test compound; and
- b) determining the effect of the test compound on the activity of the polypeptide to thereby identify a compound which modulates the activity of the polypeptide.

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23. A method for treating a subject having a pain disorder characterized by aberrant TWIK activity or aberrant TWIK nucleic acid expression comprising administering to the subject a TWIK modulator in an amount sufficient to treat the pain disorder, thereby treating said subject having a pain disorder.

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24. The method of claim 23, wherein the TWIK modulator is a small molecule.

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25. The method of claim 23, wherein the pain disorder is hyperalgesia.

26. The method of claim 23, wherein the pain disorder is headache.

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27. The method of claim 23, wherein said TWIK modulator is administered in a pharmaceutically acceptable formulation.

28. The method of claim 23, wherein said TWIK modulator is administered using a gene therapy vector.

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29. The method of claim 23, wherein the TWIK modulator is capable of modulating TWIK polypeptide activity.

30. The method of claim 29, wherein the TWIK modulator is an anti-TWIK antibody.

31. The method of claim 29, wherein the TWIK modulator is a TWIK polypeptide comprising the amino acid sequence of SEQ ID NO:2, or a fragment thereof.

32. The method of claim 29, wherein the TWIK modulator is a TWIK polypeptide comprising an amino acid sequence which is at least 90 percent identical to the amino acid sequence of SEQ ID NO:2, wherein said percent identity is calculated using the ALIGN program for comparing amino acid sequences, a PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.

33. The method of claim 29, wherein the TWIK modulator is an isolated naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of SEQ ID NO:2, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to a complement of a nucleic acid molecule consisting of SEQ ID NO:1 at 6X SSC at 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65°C.

34. The method of claim 23, wherein the TWIK modulator is capable of modulating TWIK nucleic acid expression.

35. The method of claim 34, wherein the TWIK modulator is an antisense TWIK nucleic acid molecule.

36. The method of claim 34, wherein the TWIK modulator is a ribozyme.

37. The method of claim 34, wherein the TWIK modulator comprises the nucleotide sequence of SEQ ID NO:1, or a fragment thereof.

38. The method of claim 34, wherein the TWIK modulator comprises a nucleic acid molecule encoding a polypeptide comprising an amino acid sequence which is at least 90 percent identical to the amino acid sequence of SEQ ID NO:2, wherein said percent identity is calculated using the ALIGN program for comparing amino acid sequences, a PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.

39. The method of claim 34, wherein the TWIK modulator comprises a nucleic acid molecule encoding a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, wherein the nucleic acid molecule which hybridizes

to a complement of a nucleic acid molecule consisting of SEQ ID NO:1 at 6X SSC at 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65°C.